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determining the presence of said prion according to the degree of interaction between the ligand and the prion present in the TSE-infected B cell and TSE-infected T cells.

REMARKS

The following is in response to the Office Action, which was made final and mailed July 09, 2002, in the above identified application. Claims 35-40 currently are pending. The Examiner rejected all claims under 35 U.S.C. § 102(b), § 112 second paragraph, and § 103(a).

Claims 35-40 have been amended to address the Examiner's concerns. Applicants provide a marked up version of the claims, attached herewith, showing where the amendments were made. No new matter has been added as a result of these amendments. Applicants respectfully submit that the Amendments place claims in a better form for appeal, and respectfully request entry of the amendments into the record.

Applicants are also providing the corrected version of the drawings and respectfully request entry of these drawings into the record.

Rejection under 35 U.S.C. §112, second paragraph.

A) Claims 35-37 are rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

To meet the requirements of 35 U.S.C. § 112, second paragraph, an Applicant must: first, clearly set out the boundaries of the subject matter for which protection is sought in the application, and second, Applicant must claim whatever he regards as his invention. All what is required is that the claims set out and circumscribe a particular area which Applicant regards as the invention with a reasonable degree of precision and definiteness, and not encompassing more than what Applicant regards as his invention. *In re Borkowski* 164 USPQ 642,646, 1970.

To comply with both requirements and to obviate the Examiner's rejection, Applicants have amended claims 35-37 to include sufficient number of steps in order to describe a "test".

Support for the amendments are found in the specification. Example 4 (pages 77-81) and Example 5 (pages 81-82) specifically describe the production and purification of monoclonal and polyclonal antibodies against TSE-infected B-cells and T-cells. Examples 6 thorough 9 (pages 82-86) describe different assays in which the specific antibody-antigen reaction can be carried out, i.e., Western blotting, EIA Microtiter assay, Microparticle Enzyme Immunoassay.

Additionally, the specification discloses as part of Applicants' invention, an antibody directed to specific antigens (markers) in TSE-infected B cells and TSE-infected T cells, and the use of said antibody in a diagnostic assay (page 37, second and third paragraphs, and page 38, fifth and sixth paragraphs).

Therefore, Applicants submit that when read in light of the specification, the amended claims adequately point out and distinctly set out the boundaries of the subject matter that the Applicants regard as the invention.

In view of the above discussion, Applicants respectfully submit that the rejection of claims 35-37 as indefinite under § 112 has been overcome and request its withdrawal.

B) Claims 38-40 are rejected under 35 U.S.C. § 112, second paragraph, as ambiguous for failing to identify what the "ligand" is defining.

To obviate the Examiner's rejection, Applicants have amended claims 38-40 to clearly indicate that the ligand is an antibody that detects the prions carried by the TSE-infected B cells or TSE-infected T cell. Support for the amendments can be found in Example 11 (page 93-94) which describes, a) how infectivity of B cells and T cells can be related to their ability to sustain prion replication, and b) the immunoblots analysis and immunocytochemistry involved using anti-PrP antibodies (pages 109-110).

In view of the aforementioned amendments, reconsideration and withdrawal of the § 112, second paragraph rejection of claims 38-40 is respectfully requested.

Rejection of claims 35-37 under 35 U.S.C. §102(b)

The Examiner contends that claims 35-37 are anticipated by Kuroda *et al.* Applicants respectfully disagree. Courts have interpreted invalidity for anticipation as requiring that all the elements and limitations of the claims be found within a single prior art reference, i.e., that there must be no difference between the claimed invention and the reference disclosed, as viewed by a person skilled in the art.

Applicants respectfully submit that the Kuroda *et al.*, reference fails to meet the claimed invention. Kuroda *et al.*, teaches a method to determine the infectivity of spleen T cells and B cells from CJD infected animals. The infectivity was determined by inoculating lymphocytes from virus-infected animals into recipient animals. According to the number of infected recipient, dead animals, length of incubation period, and other parameters, Kuroda *et al.*, concluded that the CJD virus preferentially replicated in low-density lymphocytes. The Examiners correctly points out that the ability to transmit a disease to another animal is a well-established means of testing for the presence of an infectious agent (Paper 18, page 5).

However, Applicants respectfully submit that the claims of the present application refer to a method for identifying infectious B cells and T cells using a marker specifically present in TSE-infected B cells and TSE-infected T cells. The marker for TSE-infected B cells and T cells is detected by using a specific antibody, as explained in Examples 4 and 5 of the specification.

Since the teaching of Kuroda *et al.*, cannot be construed as having each and every element of Applicant's claimed invention, the reference of Kuroda *et al.*, cannot anticipate the present invention. Accordingly, reconsideration and withdrawal of the 102(b) rejection is respectfully requested.

Claims 35-37 stand rejected under 35 U.S.C. §102(b) as anticipated by Manuelidis *et al.* Applicants, respectfully disagree for the same reasons stated above. Manuelidis *et al.*, teaches a method for determining viremia in CJD by inoculating buffy coat of blood from infected animals into sane recipient animals, concluding that the disease may be transmitted by blood transfusion.

Applicants respectfully submit that the claims of the present application refer to a method for identifying infectious B cells and T cells using a marker specifically present

in TSE-infected B cells and TSE-infected T cells. The marker for TSE-infected B cells and T cells is detected by using a specific antibody, as explained in Examples 4 and 5 of the specification.

Applicants respectfully submit that since the teaching of Manuelidis *et al.*, cannot be construed as having each and every element of Applicant's claimed invention, the reference of Manuelidis *et al.*, cannot anticipate the present invention. Accordingly, reconsideration and withdrawal of the 102(b) rejection is respectfully requested.

Rejection of claims 35-40 under 35 U.S.C. §103(a)

Claims 35-37 are rejected under 35 U.S.C. §103(a) as being obvious in view of O'Rourke *et al.*, and/or Korth *et al.*, in view of Kurida *et al.*, and/or Manuelidis *et al.*

Applicants respectfully assert that the Examiner is erring as a matter of law in combining the named references to reject claims 35-40 as these references fail to teach or suggest their combination either implicitly or explicitly.

O'Rourke *et al.* disclose diagnostic assays for detecting PrP-Sc. The assay employs the third eyelid lymphoid tissue to detect PrP-Sc in ruminants (cattle, sheep, mule deer, elk, etc.) using monoclonal antibodies that bind to a conserved epitope on the ruminant PrP proteins in fixed or frozen tissue. As admitted by the Examiner, O'Rourke *et al.* fails to teach a method that involves the steps of collecting B cells and/or T cells from a test sample and then directly testing these cell types for the presence of prions associated with transmissible spongiform encephalopathy. As it stands O'Rourke's teachings do not suggest that this is applicable for humans, for example, or other animals that lack the nictitating membrane.

Korth *et al.* describe a monoclonal antibody, 15B3, which the authors claim can discriminate between the normal and disease-specific forms of PrP. As with O'Rourke *et al.*, the Examiner has admitted that Korth *et al.* fail to teach a method that involves the steps of collecting B cells and/or T cells from a test sample and then directly testing these cell types for the presence of prions associated with transmissible spongiform encephalopathy.

Kuroda *et al.* and/or Manuelidis *et al.* teach, firstly that the infective agent of transmissible spongiform encephalopathy was a virus, and secondly both references teach

that CJD may have a hematogenous way of dissemination. Collectively, these references present evidence that when blood or tissues from infected animals are inoculated in non-diseased recipients, the recipients become infected. There is nothing in these references that would suggest to one skilled in art the causal connection between B-cells and T-cells and prions associated with transmissible spongiform encephalopathy.

The cited references also fail to provide one of ordinary skill in the art with a reasonable expectation of success in achieving the claimed invention. The references mentioned above provide no expectation that the skilled in the art would appreciate that the route of infection of TSE is based on the interaction between prions and B cells and T cells, therefore on the importance of detecting infection markers or the prions in these cells, *specifically*.

Accordingly, Applicants respectfully request the withdrawal of the § 103 rejection.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If any additional fees are incurred as a result of the filing of this paper, authorization is given yo charge deposit account no. 01-0025.

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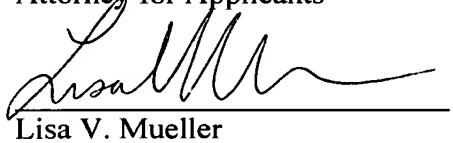

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MARKED UP VERSION OF THE CLAIMS

35. (Amended) A method of [testing]identifying TSE-infected B cells [for the presence of prions] associated with transmissible spongiform encephalopathy in a test sample, the method comprising the steps of:

obtaining a test sample;

collecting B-cells from the test sample; [and]

contacting said collected B-cells with an antibody specific for a TSE-infected B-cell antigen for a time and under conditions to allow the formation of an antibody-antigen complex; and

detecting the amount of said antibody-antigen complex indicative of diagnosis of [testing the B-cells for the presence of prions associated with] transmissible spongiform encephalopathy.

36. (Amended) A method of identifying TSE-infected T cells [testing for the presence of prions] associated with transmissible spongiform encephalopathy in a test sample, the method comprising the steps of:

obtaining a test sample;

collecting T-cells from the test sample; [and]

contacting said collected T cells with an antibody specific for a TSE-infected T cell antigen for a time and under conditions to allow the formation of a antibody-antigen complex; and

detecting the amount of said antibody-antigen complex indicative of diagnosis of [testing the T-cells for the presence of prions associated with] transmissible spongiform encephalopathy.

37. (Amended) A method of identifying TSE-infected B cell and TSE-infected T cells [to test for the presence of prions] associated with transmissible spongiform encephalopathy in a test sample, the method comprising the steps of:

obtaining a test sample;

collecting B-cells and T-cells from said test sample; [and]

contacting said B-cells and T-cells with an antibody specific for a TSE-infected B cell and TSE-infected T cell antigen for a time and under conditions to allow the formation of a antibody-antigen complex; and

detecting the amount of said antibody-antigen complex indicative of diagnosis of [testing the B-cells and T-cells for the presence of prions associated with] transmissible spongiform encephalopathy.

38. (Amended) A method for identifying the presence of prions in TSE-infected B-cells, wherein said prions are associated with transmissible spongiform encephalopathy, the method comprising the steps of:

obtaining a test sample;

collecting B-cells from said test sample;

contacting said [adding a ligand to the isolated] B-cells with a ligand, wherein said ligand is an anti-PrP antibody capable of identifying prions in TSE-infected B-cells [infected with prions] associated with transmissible spongiform encephalopathy for a time and under conditions to produce an antibody-antigen complex; and

determining the presence of said prions according to the degree of interaction between the ligand and the prion present in the TSE-infected B cell.[identifying the presence of prions associated with transmissible spongiform encephalopathy.]

39. (Amended) A method for identifying the presence of prions in TSE-infected T-cells, wherein said prions are associated with transmissible spongiform encephalopathy, the method comprising the steps of:

obtaining a test sample;

collecting T-cells from said test sample;

contacting said T cells with a ligand [adding a ligand to the isolated T-cells] wherein said ligand is an anti-PrP antibody capable of identifying prions in TSE-infected T-cells [that are infected with] associated with transmissible spongiform encephalopathy for a time and under conditions to produce an antibody-antigen complex; and

determining the presence of said prion according to the degree of interaction between the ligand and the prion present in the TSE-infected T cell.[identifying the presence of prions associated with transmissible spongiform encephalopathy.]

40. (Amended) A method for identifying the presence of prions in TSE-infected B-cells and TSE-infected T-cells, wherein said prions are associated with transmissible spongiform encephalopathy, the method comprising the steps of:

obtaining a test sample;

collecting B-cells and T-cells from said test sample;

contacting said B-cells and T-cells with a ligand, [adding a ligand to the isolated B-cells and T-cells] wherein said ligand is an anti-PrP antibody capable of identifying prions in TSE-infected B-cells and TSE infected T-cells associated with transmissible spongiform encephalopathy, for a time and under conditions to produce an antibody-antigen complex [T-cells that are infected with transmissible spongiform encephalopathy]; and

determining the presence of said prion according to the degree of interaction between the ligand and the prion present in the TSE-infected B-cells and TSE-infected T-cells.[identifying the presence of prions associated with transmissible spongiform encephalopathy.]